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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/762,304	04/16/2001	Franz Josef Meyer-Almes	P66378US0	4840

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EXAMINER	
YU, MISOOK	
ART UNIT	**PAPER NUMBER**
1642	

DATE MAILED: 10/17/2002

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/762,304	MEYER-ALMES, FRANZ JOSEF	
	Examiner	Art Unit	
	MISOOK YU, Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 August 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restrictions

On reconsideration, groups I and II will be rejoined and examined as one invention and the requirement for species election of the different test substances listed in claim 3 will be withdrawn since the instant invention is to screen a substance that causes apoptosis by inducing caspase cascade in cells. Claims 1-11 are pending and examined on merits as they are drawn to the elected species of measuring apoptosis by measuring caspase activity by determining fluorgenic or chromgenic substrate turnover rate.

Priority

Acknowledgment is made of applicant's claim for foreign priority based on an application filed in Germany on 03/12/1999. It is noted, however, that applicant has not filed a certified copy of the 19910956.7 application as required by 35 U.S.C. 119(b).

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows: An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification or in an application data sheet (37 CFR 1.78(a)(2) and (a)(5)).

Specification

The instant specification at page 5, 3rd paragraph (line 3) says "Table 1" but this examiner is unable to find the table in the instant specification. Applicant is requested to point out where the table is in the specification.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-8 are rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: determination steps to accomplish the purpose stated in preamble.

Claims 1-11 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 recites "separating off the cells" but it is not clear what the metes and bounds are for the phrase.

Regarding claim 2, the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 3 is confusing because the claim does not make much sense in terms of sentence structure. Amending claim 3 to "The method according to claim 1, wherein said substance is selected from the group consisting of pharmaceutically active substances, ..., and nucleic acid hybrids" would obviate this rejection.

Regarding claim 4 the phrase "such as" renders the claim indefinite because it is unclear whether the limitations following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

Claim 5 recites "characterized in that said marker comprises" but it is not clear what the metes and bounds are for the phrase.

Claim 5 recites "a dye portion" but it is not clear what the metes and bounds are for the phrase.

Claim 5 recites "a collidal precious metal" but it is not clear what the metes and bounds are for the phrase.

Claim 5 recites "rare-earth metal chelates" but it is not clear what the metes and bounds are for the phrase.

Claim 5 recites the limitation "said marker" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 6 recites "no sooner than 10 h, especially from 24 to 48 h" but it is not clear what the metes and bounds are for the phrase. Does it mean no sooner than 24 to 48 hours after adding the test substance or after adding caspase substrate?

Claim 8 is confusing. What element(s) of claim 1 does claim 8 limit? For the purpose of this office action, this examiner will assume that method of measuring caspase activity of instant invention (claims 1-9) is measured for the purpose of classifying tumors, finding new chemotherapeutic agents, or optimizing chemotherapeutic protocols. However, this treatment does not relieve applicant the burden of responding to this rejection.

Claim 9 recites "a kit containing a sample support with sample compartments" but it is not clear what the metes and bounds are for the phrase.

Claim 9 recites "substance" but it is not clear what the metes and bounds are for the term. Is the test "substance" a substance being tested or a substrate for caspase cleavage? Since the instant invention is screening method and applicant argued in the traversal of restriction requirement that the kit is being used for the method of instant invention, this examiner will assume for the purpose of this office action that the substance is a substrate of caspase cleavage. However, this treatment does not relieve applicant the burden of responding to this rejection.

Claim 9 recites "a standardized solution of a reagent for measuring caspace activity" but it is not clear what the metes and bounds are for the phrase. Is this buffer solution? Or lysis solution? Or something else? All of them?

Claim 10 recites the limitation "said substance**s**" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 10 is confusing therefore indefinite because it says substances being present as dry substances, in solution. How could substances in solution being dry?

Claim 11 recites the limitation "said matrix" in line 1. There is insufficient antecedent basis for this limitation in the claim.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had ***possession*** of the claimed invention. Claims.

Claims 1-11 are interpreted as drawn to a kit and a method of detecting apoptosis by measuring caspase activity by measuring fluorogenic or chromogenic change of ***a genus of caspase substrate***. The specification at pages 11-13 teaches that aminocoumarin-DEVD is a caspase substrate and caspase activity can be measured using aminocoumarin-DEVD. Based on a method using only one substrate, one cannot predict the types of additional substrates that can be cleaved by activated caspace in cells undergoing apoptosis. Since the genus includes a large number of unpredictable species, possession of only one species in the method is not seen as sufficient to reasonably convey possession of the entire genus. It is concluded that applicants adequately describes the method of measuring caspase activity using aminocoumarin-DEVD only.

Claims 1-11 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the method using aminocoumarin-DEVD, does not reasonably provide enablement for any other fluorogenic or chromgenic substrate in the instant invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly

connected, to make the invention commensurate in scope with these claims. Claims 1-8 are interpreted as drawn a kit and a method of detecting caspase activity by measuring a fluorogenic or chromogenic change of a chemically undefined substrate for activated caspase in cells undergoing apoptosis. The specification at Fig. 1-6 and Examples 1 and 2 teaches aminocoumarin-DEVD can be used to measure activated caspases in cells undergoing apoptosis but the specification does not teach any other method of measuring caspace activity or apoptosis. The claims are broadly drawn to measuring casepase activity using undefined flourogenic and chromogenic substrate of caspase activity. The specification does not teach the specific structures responsible for caspase cleavage activity, nor provide guidance as to how to make the substrate that could be used in the method of measuring caspase activity. Considering the broad scope of the claims, and the limited teachings of the specification, it is concluded that undue experimentation would be required to enable the full scope of the claims.

Claim 8 is rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for screening for possible new chemotherapy, does not reasonably provide enablement for any other purposes listed in claim 8. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use/make the invention commensurate in scope with these claims. Claim 8 is interpreted as drawn to method of measuring apoptosis by determining caspase activity in order to stratify tumors, to optimize individual chemotherapy and to find a possible new chemotherapy. Either Benjamin et al (March 1998, Molecular Pharmacology 53, pages 446-450) or Martins et al (Dec. 1, 1997, Blood 90, pages 4285-4296) teach caspases are activated in cells undergoing apoptosis. Since the activated caspases cleave aminocoumarin-DEVD into a product that could be easily detected by a spectrometer, the instant method could be used to screen a compound causing apoptosis, activating caspase cascades. The screened

compound could be further tested if it can be used as a new chemotherapeutic agent. However, neither the art nor the specification teaches how the instant invention could be used to stratify tumor diseases or optimize individual chemotherapy. Considering the broad scope of the claims, unpredictability in the art, and the limited teachings of the specification, it is concluded that undue experimentation would be required to enable the full scope of the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-8 are rejected under 35 U.S.C. 102(b) as being anticipated by either Benjamin et al (March 1998, Molecular Pharmacology 53, pages 446-450) or Martins et al (Dec. 1, 1997, Blood 90, pages 4285-4296).

The claims are interpreted as drawn to method of measuring apoptosis of cells by determining caspase activity in cells undergoing apoptosis, wherein the different cells tested are listed in claim 2, wherein the apoptosis of the cells are caused by a test substance listed in claim 3, wherein caspase activity are measured by fluorogenic or chromogenic signal of caspase substrate cleaved by activated caspases in cells undergoing apoptosis in claims 4 and 5, wherein the time frame is defined in claim 6, wherein the caspase activity is standardized as per cell numbers, wherein the ultimate purpose for instant invention is listed in claim 8. Benjamin et al (March 1998, Molecular Pharmacology 53, pages 446-450) teach a method of measuring apoptosis caused by at least one substance by measuring caspase activity upon disruption of the cells "without previously separating off cells" at page 4284 under Materials and Methods, Figures 1-7, especially Fig. 5. Martins et al (Dec. 1, 1997, Blood 90, pages 4285-4296) also

teach the instant method at page 447 under Experimental Procedures and Figs. 1-5. The references above do not separate off the cells incubated with the test substance before the casepase activity measurement using the substrate aminocoumarin-DEVD.

Claims 9-11 are rejected under 35 U.S.C. 102(b) based upon a public use or sale of the invention.

Claims 9-11 are interpreted as drawn to kit for measuring caspase activity. Note page 196 of Clontech 2000 Catalog and the last paragraph of page 5 of the instant specification.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MISOOK YU, Ph.D. whose telephone number is 703-308-2454. The examiner can normally be reached on 8 A.M. to 4:30 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony C Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

MARY E. MOSHER
PRIMARY EXAMINER
GROUP 1600

Misook Yu
October 12, 2002

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